A COMPARATIVE CLINICAL EVALUATION OF SUBGINGIVALLY DELIVERED 0.5% AZITHROMYCIN GEL AND 2 MG TETRACYCLINE HYDROCHLORIDE FIBERS AS AN ADJUNCT TO SCALING AND ROOT PLANING IN THE TREATMENT OF CHRONIC PERIODONTITIS

A Dissertation submitted in
partial fulfillment of the requirements
for the degree of

MASTER OF DENTAL SURGERY

BRANCH – II
PERIODONTICS

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY
Chennai – 600 032

2014 - 2017

CERTIFICATE BY HEAD OF THE DEPARTMENT /

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I hereby declare that this dissertation titled **"A COMPARATIVE CLINICAL EVALUATION OF SUBGINGIVALLY DELIVERED 0.5% AZITHROMYCIN GEL AND 2 MG TETRACYCLINE HYDROCHLORIDE FIBERS AS AN ADJUNCT TO SCALING AND ROOT PLANING IN THE TREATMENT OF CHRONIC PERIODONTITIS"** is a bonafide and genuine research work carried out by me under the guidance of **Dr. K. MALATHI, M.D.S.,** Professor, HOD and Guide, Department of Periodontics, Tamil Nadu Government Dental College and Hospital, Chennai -600003.

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This agreement herein after the "Agreement" is entered into on this day …… between the Tamil Nadu Government Dental College and Hospital represented by its **Principal** having address at Tamil Nadu Government Dental College and Hospital, Chennai – 600 003, (hereafter referred to as, 'the college')

And

Mrs. Dr. K. MALATHI aged 49 years working as **Professor** in Department of Periodontics, Tamil Nadu Government Dental College and Hospital, Chennai (herein after referred to as the 'Principal Investigator'),

And

Dr. S. ANNAPOORANI, aged 38 years currently studying as **Post Graduate student** in Department of Periodontics, Tamil Nadu Government Dental College and Hospital, Chennai – 600 003, (hereafter referred to as 'the PG and co-investigator')

Whereas the PG student as part of his curriculum undertakes this research on **"A COMPARATIVE CLINICAL EVALUATION OF SUBGINGIVALLY DELIVERED 0.5% AZITHROMYCIN GEL AND 2 MG TETRACYCLINE HYDROCHLORIDE FIBERS AS AN ADJUNCT TO SCALING AND ROOT PLANING IN THE TREATMENT OF CHRONIC PERIODONTITIS"** for which purpose the Co-investigator and the college shall provide the requisite infrastructure based on availability and also provide facility to the PG student as to the extent possible as a principal investigator.

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APPROVAL FROM INSTITUTIONAL ETHICS COMMITTEE TO PROCEED WITH THE RESEARCH WORK

Title of the work: A Comparative clinical evaluation of Subgingivally delivered 0.5% Azithromycin Gel and 2mg. Tetracycline Hydrochloride fibers as an adjunct to scaling and root planning in the treatment of Chronic Periodontitis

Principal Investigator: Dr.S. Annapoorani
II year , MDS

Department : Department of Periodontics
Tamil Nadu Govt. Dental College & Hospital , Chennai-3

Thank you for submitting your research proposal , which was considered at the Institutional Ethics Committee meeting(IEC) held on the 6th. February 2015, at TN Govt. Dental College and the documents related to the study referred above were discussed and the modifications done as suggested and reported to us through your letter dated 02-04-2015 have been reviewed.

The decision of the members of the committee , the secretary and the Chairperson IEC of TN Govt. Dental College is here under:

Approved	Approved and advised to proceed with the study
Approved with suggestions	----------
Revision	----------
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ABSTRACT

BACKGROUND: The goal of periodontal treatment is to suppress or eliminate putative subgingival periodontal pathogens. Local delivery of antimicrobials in sustained or controlled delivery systems is used to enhance the effect of non surgical therapy. The purpose of the present study is to investigate the effectiveness of subgingivally delivered 0.5% Azithromycin gel and 2 mg of tetracycline hydrochloride fibers as an adjunct to SRP in the treatment of chronic periodontitis.

AIM: To compare the clinical effectiveness of subgingivally delivered 0.5% Azithromycin gel and 2 mg of tetracycline hydrochloride fibers in the treatment of chronic periodontitis with Non-surgical periodontal therapy.

METHODS: A total of 60 patients were selected randomly and divided into 3 groups (SRP, SRP+AZM Gel, SRP+Tetracycline Fiber). Clinical parameters such as plaque index, sulcus bleeding index, probing pocket depth and clinical attachment level were recorded at baseline, 1 month, 2 months and 3 months post operatively.

RESULTS: Significant reduction in mean pocket depth and gain in attachment level was observed in AZM gel and Tetracycline fiber group as compare to baseline but there was no significant difference between the two groups at three months. Greater percentage of reduction in clinical parameters is observed for AZM gel group than Tetracycline fiber group at three months but it was statically not significant.

CONCLUSION: All the three modalities of treatment were efficient in improving the clinical parameters and there is no statistically significant difference between AZM & Tetracycline group. In future, clinical trials with larger samples and long- term follow-up period may be employed to further explore the potential benefit of AZM as a local drug delivery agent.

KEYWORDS: Azithromycin gel, local drug delivery, chronic periodontitis, Tetracycline fibers.

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LIST OF ABBREVIATIONS

AZM	Azithromycin
CAL	Clinical Attachment Level
CEJ	Cemento–Enamel Junction
GCF	Gingival Crevicular Fluid
LDD	Local Drug Delivery
PI	Plaque Index
PLGA	Poly Lactic-Co Glycolic Acid
PPD	Probing Pocket Depth
SBI	Sulcus Bleeding Index
SRP	Scaling and Root Planing
SD	Standard deviation

INTRODUCTION

Periodontitis is an inflammatory disease which causes destruction of the tooth supporting tissues which is characterized by multifactorial etiology with pathogenic bacteria being primary etiologic agents that harbours subgingival area.[8]

The clinical signs include changes in the morphology of gingival tissues with gingival bleeding and periodontal pocket formation. This pocket makes an ideal environment for the growth and proliferation of anaerobic pathogenic bacteria.[22] Hence the treatment of periodontal disease is based on the eradication of gingival inflammation, elimination of bleeding, reducing pocket depth and arrest of the progressive destruction of soft tissue and bone. The increasing knowledge of anaerobic bacteria as predominant agents in the development of periodontal disease has led to new treatment strategies. Therapeutic approach for periodontitis may be non-surgical, surgical or combination of both.

However, mechanical therapy by itself may not always reduce or eliminate the pathogenic bacteria completely because of their inaccessible location to periodontal instrumentation. Moreover, recolonization of pathogenic bacteria occurs from the residual bacterial reservoir in dentinal tubules causing renewal of the inflammatory condition. ***(Ram TE and Slots T)*** [58]

To overcome these problems, the addition of antimicrobials both locally and systemically would augment a treatment protocol and serve as an adjunct to mechanical therapy. Systemic use of antimicrobials has adverse effects such as drug toxicity, acquired bacterial resistance, drug interaction and patient's compliance ***(Golomb G et al., 1984[16], Steinberg D, 1990)[69]***

Local delivery of antibacterial agents into periodontal pockets overrides these short comings. This mode of drug delivery avoids most of the problems associated with systemic therapy, limiting the drug to its target site and hence achieving a much higher concentration. ***(Yeung F. Is et al., 1983)[78]***Some of the antimicrobials available as local drug delivery systems are Tetracycline fibers, Metronidazole gel ,Minocycline ointment and microspheres, Chlorhexidine chip and Doxycline hyclate etc.

Tetracyclines are broad spectrum antibiotics with characteristics of collagenase inhibition, anti-inflammatory action and inhibition of bone resorption. ***(Walker 1996)[76]*** Azithromycin is effective against periodontal pathogens like *Aggregatibacter Actinomycetemcomitans* and *Porphyromonas gingivalis*. ***(Peters DH et al 1992)[55]***

So, the present study has been undertaken to compare the clinical evaluation of subgingivally delivered 0.5% Azithromycin gel and 2 mg of Tetracycline hydrochloride fibers as an adjunct to scaling and root planing in the treatment of chronic periodontitis.

AIM AND OBJECTIVES

AIM:

To compare the clinical effectiveness of subgingivally delivered 0.5% Azithromycin gel and 2 mg of tetracycline hydrochloride fibers in the treatment of chronic periodontitis with Non-surgical periodontal therapy.

OBJECTIVES:

- To compare the clinical parameters before and after the treatment in each group.
- To compare the clinical parameters between three groups.

REVIEW OF LITERATURE

Periodontal diseases comprises a group of oral infections whose primary etiological factor is dental plaque. Altering the cause is the primary aim of both non-surgical and surgical treatment regimens which now exist. Mechanical debridement of pockets by Scaling and Root Planing (SRP) is the gold standard in the management of periodontitis ***(Hung & Douglass 2002)***[29]. The ineffective nature of the mechanical debridement has led to the widespread use of antimicrobials as an adjunct to mechanical debridement ***(Quirynen et al., 2002***[57]***, Bonito et al., 2005***)[5]**.**

Limitations of Mechanical Debridement: ***(Caffesse 1986, Greenstein 2000)***[6, 22, 24]

- Unfavorable anatomy
- Intraoral microbial translocation
- Tissue invasive organisms
- Bacterial invasion into dentinal tubules ***(Quirynen et al 2002)***[57]

Chemotherapy in treatment of Periodontal Diseases:

- The use of antimicrobials offers a method to overcome limitations of mechanical therapy for the periodontal diseases. The products that are used to prevent and treat periodontal disease include mouth rinses, dentifrices, systemic antimicrobials and locally delivered antimicrobials.

- Antioxidative actions of tetracycline, doxycycline, chlorhexidine and essential oils may be a part of the mechanism of actions of chemotherapeutics used in the treatment of periodontal disease ***(Quirynen M, 2002)***[57]
- Chemotherapeutic rinses will penetrate the outer layer of the mature biofilm but at the same time the mouth rinses may not reach deep into periodontal pockets.
- In shallow and moderate pockets the use of irrigators with blunt ended cannulae are used and it may improve the ability of the drug to reach the site.
- During infection the crevicular flow volume is increased and results in further dilution and displacement of locally delivered chemotherapeutics.

Local Drug Delivery

Both typical drug delivery and controlled drug delivery are known as local drug delivery/Site specific drug delivery. ***Goodson et al., in 1979***[14] – first proposed the concept of controlled delivery in the treatment of periodontitis.

Ideal Requisites of Local Drug Delivery

- Must deliver the drug to the base of the pocket
- Must have microbiologically effective concentrations in the pocket
- It should be present for sufficient period of time
- Little or no effect on host tissues ***(Goodson 1985)***[19]
- Retentive after placement
- Ease of placement & cost effective
- Bio degradable ***(Greenstein & Polson 1998)***[23]

Indications

- As an adjunct to root surface instrumentation in pockets of 5mm or greater
- Localized recurrent pockets in patients under supportive periodontal therapy
- Non responding sites to conventional therapy in well motivated patients

Advantages of LDD *(Ram T, Slot J, 1996)*[3]

- LDD allows the use of concentration of approximately 100 times higher than does systemic administration
- Site specific
- Controlled release of delivery systems have allowed us to administrative therapeutic levels of drugs on the site of infection for prolonged period of time

Studies related to Local Drug Delivery

The efficacy of local adjuvant therapy was supported in **2003** by an international workshop ***(Hanes PJ, Purins JP)***[27] which concluded that the clinical result obtained following SRP that includes adjunctive use of a locally delivered, sustained release chemotherapeutics is significantly enhanced in comparison with that following SRP alone.

Bonito et al., 2005[5] revealed that adjunctive use of local antimicrobials shows significant beneficial effect.

Tonetti et al., 1995[70], ***Dannewitz et al., 2009***[7] managed the furcation defects with local delivery devices. They found that short term (3-6 months) adjunctive benefits in controlling gingival inflammation as well as improvements in probing depths and clinical attachment level.

Esposito et al., 2012[12], ***Muthukuru et al., 2012***[46] managed peri- implantitis by using local delivery device. They identified that local delivery combined with subgingival debridement has better improvement than subgingival debridement alone.

Matesanz Perez et al., 2013[40] in their systematic review and meta analysis concluded that local delivery of antimicrobials along with scaling and root planing results in significant improvement in clinical parameters.

Zaugg B et al., 2014 in his meta-analysis concluded that adjunctive local or systemic measures seem to improve the classic non-surgical periodontal therapy, i.e., scaling and root planing.

Drugs used for Local Drug Delivery

- Tetracycline
- Doxycycline (Atridox)
- Minocycline (Arestin)
- Metronidazole (Elyzol)
- Chlorohexidine
- Azithromycin

Newer Trends *(Jyoti Pattanshetti et al., 2016)*[31]

- Taurolidine
- Simvastatin
- Alendronate
- Basic fibroblast growth factor
- Chitosan
- Ipriflavone

Tetracycline

Tetracycline comprises a group of broad spectrum antimicrobial agents that were introduced into clinical practice in the late 1900's. These are:

- Primarily bacteriostatic agents but has bactericidal effect in higher concentration ***(Walker 1996)*** [25]
- Inhibit protein synthesis by binding to 30S ribosomes in susceptible organism
- In addition to its antimicrobial action, it also possess the following function
    - Collagenase inhibition
    - Anti-inflammatory action
    - Inhibition of bone resorption
    - Demineralizes dentin, cementum and dentin-cementum when applied topically thereby enhancing attachment of fibroblasts to the tooth surface (***Wikesjo et al., 1986***[77]***, Morrison et al., 1992)***[45]

- Has high substantivity (ie.,) after local delivery, it has been detected at 1-20 µm within epithelial tissues ***(Giancio et al., 1992)***[14]
- Detectable in crevicular fluid several weeks following application ***(Wikesjo et al., 1986)***[77]
- Attains high concentration in crevicular fluid

Tetracycline Fibers (Actisite®)

- FDA approved system
- Non-resorbable cylindrical drug delivery devices made of biologically inert, plastic co-polymer loaded with 25% tetracycline hydrochloride powder
- 23 cm in length, 0.5 cm in diameter
- The fiber is flexible and can be folded on itself to nearly fill the pocket
- Able to release and maintain tetracycline for a period of 7 days ***(Tonetti et al., 1990)***[70] with mean concentration of 43 µg/ml in the superficial portions of the pocket wall

Periodontal Plus AB® is a bio-resorbable tetracycline fiber contains tetracycline hydrochloride (2mg of tetracycline) in which 25mg of collagen fibrils that can be directly applied for all levels of periodontal infections. This fiber offers the advantage of no second appointment for removal.

Studies Regarding Tetracycline Fibers:

Goodson et al., 1979[18] observed that tetracycline filled hollow fibers placed in the gingival sulcus had dramatic effect collectively on the periodontal micro flora and progression of clinical manifestation of disease. Other importance lies in the effective elimination of spirochetes from the gingival sulcus by means of a single placement of tetracycline filled hollow fibers and these eliminated spirochetes from the diseased site do not recolonize in spite of the persistence of viable organisms anywhere else in the mouth.

Lindhe 1979 et al.,[36] in his experiments demonstrated that use of tetracycline filled hollow fiber devices markedly changes the composition of subgingival flora of initially diseased periodontal sites.

Chopra et al., 1985 stated that tetracycline is bacteriostatic inhibitors of protein synthesis. They accumulate intracellularly by way of energy dependent transport systems present in bacterial membrane.

OÇonnel BC et al., 1990[49] reported that strict anaerobic bacteria are susceptible to tetracyclines, although some black-pigmented bacteroides have been reported to be minocycline-resistant.

Goodson et al., 1991[20] in his longitudinal trial evaluated tetracycline fiber vs placebo fiber Vs scaling and root planing and no treatment. Significant improvement is observed in all the periodontal parameters in tetracycline fiber.

Morrison et al., 1992[45] stated that scaling and root planing using tetracycline fibers resulted in significant improvement than scaling and root planing alone.

Newman et al., 1994[47] in longitudinal trial showed that SRP vs SRP + tetracycline fibers in maintenance patients, results in significant clinical improvement including attachment levels at 1, 3, and 6 months than SRP alone.

Michalowicz et al., 1995[43] showed that SRP in conjunction with fibers for 10 days can significantly reduce disease recurrence at 3-12 months following treatment.

Bernimoulin et al., 1996[48] compared the application of tetracycline fibers with systemic administration of amoxicillin-clavulanate potassium. Their results showed no difference in clinical results between the groups, also supported by ***Noyan et al., 1997***[48] **and** ***Drisko et al., 1993***[9].

Tonetti et al., 1998[71] did a study on tetracycline fiber therapy for treating mandibular class 2 furcation and clinical outcome were evaluated at 3 and 6 months. At 3 months the combined treatment was significantly better than mechanical therapy done alone.

Friesen et al., 2002[13] showed local delivery of tetracycline has better clinical outcome than root planing alone in reducing probing depth and bleeding on probing.

Pavia et al., 2003[54] showed that tetracycline and its derivatives minocycline, oxytetracycline and chlortetracycline strongly absorb to tooth surfaces which retain their antibacterial activity and efficient in treating chronic periodontitis.

Rutger Persson 2006 et al.,[61] Local delivery with tetracycline fibers has also a role to play in the treatment of periimplantitis sites as observed in microbiologic studies.

In **2004, *Rodrigues et al.,*[60]** compared antibiotic resistance profile with local and systemic tetracycline administration and observed that bacterial resistance is less in locally delivered tetracycline.

***Panwar and Gupta, 2009*[53] and *Kataria et al., 2015*[32]** applied tetracycline fibers as an adjunct to SRP found to be more effective in reducing inflammation.

***Sachdeva and Agarwal, 2011*[62]** applied tetracycline in the form of modified collagen matrix followed SRP and found beneficial role in treatment of chronic periodontitis.

***Munishwar Singh et al., 2014*[66]** in his study concluded that SRP plus Tetracycline fiber group showed better optimum clinical results in comparison to clinical results in comparison to the control group and SRP plus Chlorhexidine group.

Azithromycin (AZM):

- Semi synthetic and stable antibiotic
- Macrolide act as anti-inflammatory agents as well as antimicrobial agents ***(Maizumi N, 2002)*[38]**
- Azithromycin is the first subclass of macrolides called azalides ***(Walker 1996)*[76]**
- It shows good bacteriostatic in vitro activity against a wide variety of organisms found in mouth (***Sefton AM, 1996***)[63]
- It has a wide antimicrobial spectrum of action towards anaerobic bacteria as well as Gram negative bacilli (***Peters DH et al., 1992***)[55]
- Interfere with bacterial protein synthesis by binding to 50 s ribosomal unit.

- It is effective against periodontal pathogens like *Aggregatibacter actinomycetemcomitans* and *Porphyromonas gingivalis*. So it is used in the treatment of periodontal infections ***(Pajukanta R, 1993)***[51,52]
- AZM is successfully used in ophthalmology[34], dermatology[42] and to treat acute respiratory infection.
- It has no effect on hepatic cytochrome p450 enzyme[28]**.**
- This drug is safe, even in pregnancy, lactation and in children.
- Azithromycin has significantly less bacterial resistance to the subgingival microflora of chronic periodontitis compared to other commonly prescribed antibiotics ***(van Winkelhoff AJ, 1999)***[74]
- Long half-life and good tissue penetration.
- Characterized by its significantly higher uptake by fibroblasts and acute-phase reactant cells such as polymorpho neutrophils, monocytes and lymphocytes.
- The drug is subsequently delivered and released in higher concentrations to phagocytosed bacteria at the site of infection ***(Blandizzi C, 1999, McDonald PJ, 1991)***[4, 41].

Studies regarding Azithromycin:

Smith et al., 2002[67] compared the clinical effects of SRP plus placebo to SRP plus systemic AZM. SRP + AZM was better improving clinical parameters such as pocket depth and bleeding on probing.

Mascarenhas et al., 2005[39] used AZM plus SRP in the treatment of moderate to severe periodontitis in smokers provided significantly greater probing depth reduction and clinical attachment gain at moderate and deep pockets 6 months post-therapy than SRP alone.

Gomi et al., 2007[17] used systemic administration of AZM in conjunction with SRP demonstrate reduction in probing depth. But total number of bacteria did not change during examination.

Pradeep et al., 2008[1] evaluated the effect of subgingivally delivered 0.5% AZM in the treatment of chronic periodontitis as an adjunct to scaling and root planing observed significant reduction in probing depth.

Oteo et al., 2010[50] – SRP plus AZM 500 mg for 3 days improves all the clinical parameters in the treatment group.

Tyagi et al., 2011[72] investigated the clinical effectiveness of AZM at a concentration of 0.5% in an indigenously prepared, bioabsorbable and controlled release gel is used to enhance the effectiveness of non-surgical mechanical debridement in the treatment of chronic periodontitis.

Han et al., 2012[26] reported no significant difference in clinical attachment level of sites with 4-6 mm pocket by adjunctive use of AZM with non-surgical periodontal therapy in chronic periodontitis.

Emingil et al., 2012[11] studies SRP plus AZM (500 mg for 3 days) compared to SRP + Placebo (3 days) with the 3 and 6 months follow-up, all clinical parameters improved.

Sayyed et al., 2012[64] suggested that adjunctive use of systemic AZM show significant clinical benefit in the treatment of chronic periodontitis.

Pradeep et al., 2013[56] compared SRP plus 0.5% AZM gel with SRP plus placebo at 3, 6 and 9 months interval. He found that significant improvement in the treatment group compared to placebo group. No improvement in bleeding on probing.

Antonio Rentus et al., 2016[2] in his systematic review and meta-analysis shown that the systemic administration of AZM has better beneficial effect compared with SRP on its own for the treatment of chronic periodontitis.

MATERIALS AND METHODS

Source:

The study population selected from the outpatient section of the Department of periodontitis, Tamilnadu Government Dental College and Hospital, Chennai.

Subjects:

A total of 60 patients suffering from chronic periodontitis were selected and divided into 3 groups based on intervention with 20 patients in each group.

Age group: 30-45 years & **Sex:** Either sex

Group I: Only Scaling and Root Planing (SRP)

Group II: SRP + 0.5% Azithromycin gel

Group III: SRP + 2 mg Tetracycline fibers

INCLUSION CRITERIA:

- Patients with age group between 30-45 years.
- Systemically healthy patients having with probing pocket depth of ≥5mm at isolated sites.
- Patients who have not undergone any type of regenerative periodontal therapy over a period of six months prior to the initial examination.
- Patients without any antibiotic treatment in last six months.
- Patients with established willingness and ability to perform adequate oral hygiene.

EXCLUSION CRITERIA:

- Patients with known or suspected allergy to the macrolide and tetracycline group
- Patients who are suffering from any known systemic diseases or immuno-compromised
- Patients who had received any surgical or non-surgical therapy six months prior to the start of the study
- Patients who had received any antibiotic therapy in the last six months
- Tobacco users and alcoholics were excluded
- Pregnant and lactating females were not included in the study.

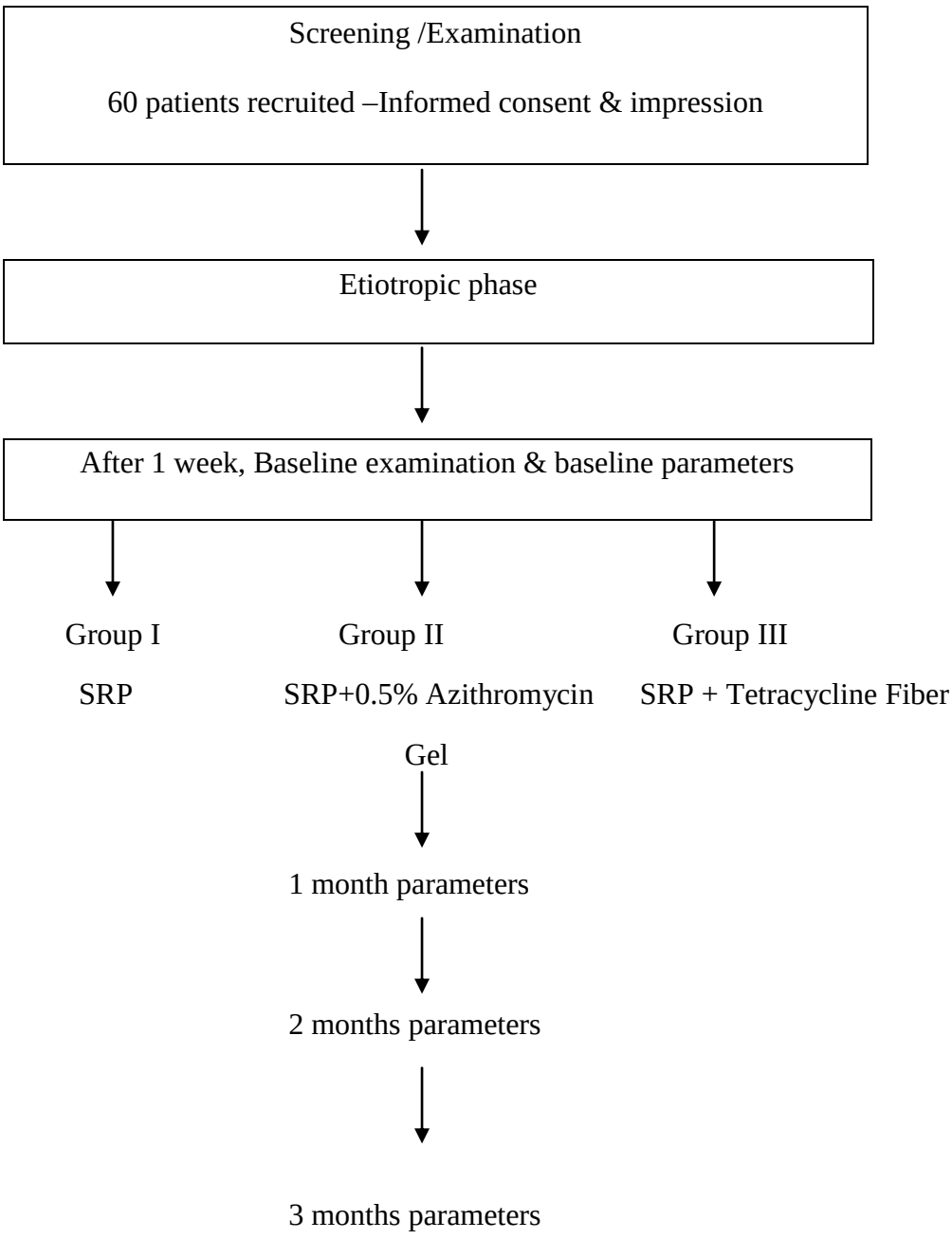
STUDY DESIGN:

The study is of randomized controlled trial type. The study participants were recruited prospectively in this study.

Ethical clearances were obtained from the Institution Ethical Committee and the ethical principles were meticulously followed throughout this study. Subjects for the study were selected randomly if they were full-filling inclusion criteria, with no discrimination on the basis of sex, caste, religion or socio-economic status as long as they were ready to follow oral hygiene instruction.

After detailed explanation of the procedure its risk and advantage, written informed consent is obtained from all the subjects selected for the study. Clinical examination is preceded by detail dental and medical history.

Study Outline:



CLINICAL PARAMETERS:

PLAQUE INDEX *(Silness and Loe., 1964)*[37]

A tooth was examined at 4 sites each (disto-facial, facial, mesio-facial, lingual/palatal)

Criteria for Scoring

Score 0	– No plaque
Score 1	– Plaque not visible to the naked eye, detected by explorer
Score 2	– Thin to moderate accumulation of soft deposits within the gingival pocket or on tooth, visible to the naked eye
Score 3	– Abundance of soft matter within the gingival pocket and/or on the gingival margin and adjacent tooth surface

Calculation

Plaque index for a tooth = Total score from 4 areas of each tooth/ 4

Plaque index for the individual = Total Plaque index of each tooth / Number of teeth examined

Interpretation of Plaque index score

0 – Excellent oral hygiene

0.1 to 0.9 – Good oral hygiene

1.0 to 1.9 – Fair oral hygiene

2.0 to 3.0 - Poor oral hygiene.

Sulcus Bleeding index: (*Muhlemann and Son, 1971*)[3]

Sulcus Bleeding Index (SBI) is performed through gentle probing of the orifice of the gingival crevice. Bleeding after probing to the base of the probable pocket is recorded.

Criteria for Scoring

Score 0 – gingival of normal texture and colour, no bleeding;

Score 1 – gingival apparently normal, bleeding on probing;

Score 2- bleeding on probing, change in colour, no oedema;

Score 3- bleeding on probing, colour change, mild oedema

Score 4- either:

a) bleeding on probing, colour change, obvious oedema

b) bleeding on probing, obvious edema

Score 5 - bleeding on probing and spontaneous bleeding, change in colour, marked oedema

Calculation

Sulcus Bleeding index for a tooth = Total score from 4 areas of each tooth/ 4 Sulcus Bleeding index for the individual = Total Sulcus Bleeding index of each tooth / Number of teeth examined.

PROBING POCKET DEPTH[21]

Probing Pocket Depth (PPD) was measured in millimeters (mm) from the gingival margin to the base of the pocket using William's Periodontal Probe. The probe was passed within the gingival sulcus along the circumference of the tooth.

Three measurements were made on the buccal aspect and three on the lingual aspect of each tooth – total of six sites per tooth ie., Mesiobuccal, Midbuccal, Distobuccal, Mesiolingual, Midlingual, Distolingual.

CLINICAL ATTACHMENT LEVEL[21]

Clinical Attachment Level (CAL) was measured in mm from the Cemento–Enamel Junction (CEJ) to the base of the pocket using William's Periodontal Probe.

- When the gingival margin was located on the anatomic crown, the level of the attachment was determined by subtracting from the probing pocket depth, the distance from the gingival margin to the CEJ. If both were the same, the loss of attachment was calculated to be zero.
- When the gingival margin coincided with the CEJ, the loss of attachment was calculated as equaling the probing pocket depth.
- When the gingival margin was located apical to the CEJ, the loss of attachment was greater than the probing pocket depth and therefore the distance between the CEJ and the gingival margin were added to the PPD.

Three measurements were made on the buccal aspect and three on the lingual aspect of each tooth – total of six sites per tooth (Mesiobuccal, Midbuccal, Distobuccal, Mesiolingual, Midlingual, and Distolingual).

The pocket probing depth and clinical attachment level measurements are standardized by using the customized acrylic stent.

Stent Preparation:

Acrylic occlusal stents were fabricated over the study models. Self cured acrylic was used for the purpose. The stent covered the occlusal and coronal 1/3rd of the labial and lingual surfaces of the tooth. It covered one tooth mesially and one distally to the study tooth. Vertical grooves made to guide the placement of the probe in the same plane and direction to avoid any variation during subsequent measurements.

STUDY PROTOCOL:

- Approval of Institutional ethical committee
- Medical history of participants and informed consent
- Complete intra oral evaluation
- Periodontal examination using clinical parameters namely Plaque Index, Bleeding Index, Probing Pocket Depth and Clinical attachment level
- Clinical photographs
- Procedure: Scaling and Root Planing in Group 1, SRP + 0.5% Azithromycin gel in Group 2, SRP + 2mg Tetracycline fibers in Group 3
- Clinical evaluation at baseline, 1 month, 2 months and 3 months after treatment.

Armamentarium:

- Mouth mirror
- Williams periodontal probe
- Dental tweezers
- Ultra Sonic Scalers
- Scalers & curettes
- Disposable syringe
- Local anesthetic solution
- Surgical gloves
- Kidney tray
- Sterile gauze & cotton
- Mouth mask

Drugs Used:

Tetracycline:

The tetracycline fiber is available in market as **Perioplus AB®** [*Advanced Biotech Products (P) Ltd.,*] as vials with tetracycline impregnated collagen fibers. These fibers are available in brownish in color and they are resorbable in nature. They are soaked in saline and packed into the periodontal pockets using blunt instrument until the pocket is filled upto or slightly below the gingival margin. COE pack® was given for the retention of the fiber. The patients were instructed not to brush or floss for seven days. They were advised to rinse with 0.2% chlorhexidine rinse twice a day.

Azithromycin Gel:

The formulation of 0.5% Azithromycin *in situ* Gel was developed in **Department of Pharmaceutics, Madras Medical College, Chennai.**

Constituents for Azithromycin *in situ* Gel preparation:

- Azithromycin dry powder (**Zota Pharmaceuticals**, Ambattur, Chennai)
- Poly Lactic co Glycolic Acid 75:25 (PLGA) with molecular weight 66,000 – 107,000 (**SIGMA-ALDRICH®**, UK)
- 1-Methyl - 2 pyrrolidone (Bio compatible solvent)

Steps in Azithromycin Gel preparation:

Buffer solution preparation:

Buffer solution is prepared by adding 27.218 g of potassium dihydrogen phosphate and 8 g of sodium hydroxide in 1 litre of distilled water which give pH of 6.8±0.2.

Preparation of drug solution:

From that buffer solution, the corresponding drug solution purity is analyzed using U.V. spectrophotometer. The established wavelength of the Azithromycin is determined as 215nm.

This is used as reference for calibrating the absorbance of drug, from which the concentration of drug in the solution is calculated.

Calibration Curve:

The amount of AZM present in a capillary tube was determined by comparing the peak response of the standard and sample of AZM solution.

Formulation of 0.5% AZM in situ Gel:

PLGA in situ gel was prepared as described by ***Shah et al., 1993***[65]**.** The weighed amount of PLGA was placed in a glass vial. Then the required amount of biocompatible solvent (1-methyl-2-pyrrolidone) was added. The vial was heated to 60℃ and agitated using a mechanical shaker to obtain a homogenous solution. Accurately weighed quantity of AZM was added to the above polymer solution and dissolved completely to obtain a homogeneous phase.

STUDY PROCEDURE:

- Under local anesthesia, all subjects will receive thorough Scaling and Root Planing (SRP) with ultrasonic scaler and Gracey curettes.
- Among them, 20 subjects will receive 0.2ml of Azithromycin gel which was injected into the test sites using a blunt cannula.
- Another 20 subjects will receive Tetracycline fibers which are inserted into the periodontal pocket until the pocket is filled. The fibers are retained by pack
- The clinical evaluation will be performed at baseline, one month, two months and three months after the procedure.

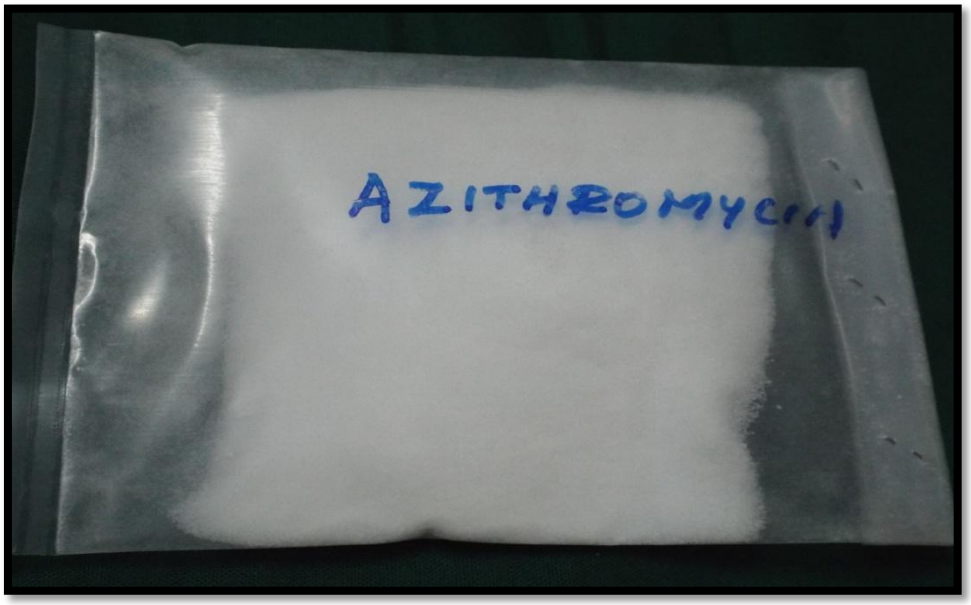
Post-Operative Instructions

- To refrain from chewing hard or sticky foods, brushing near the treated areas or using any inter-dental cleaning aids for one week.
- During the follow up period, oral hygiene maintenance was reinforced.

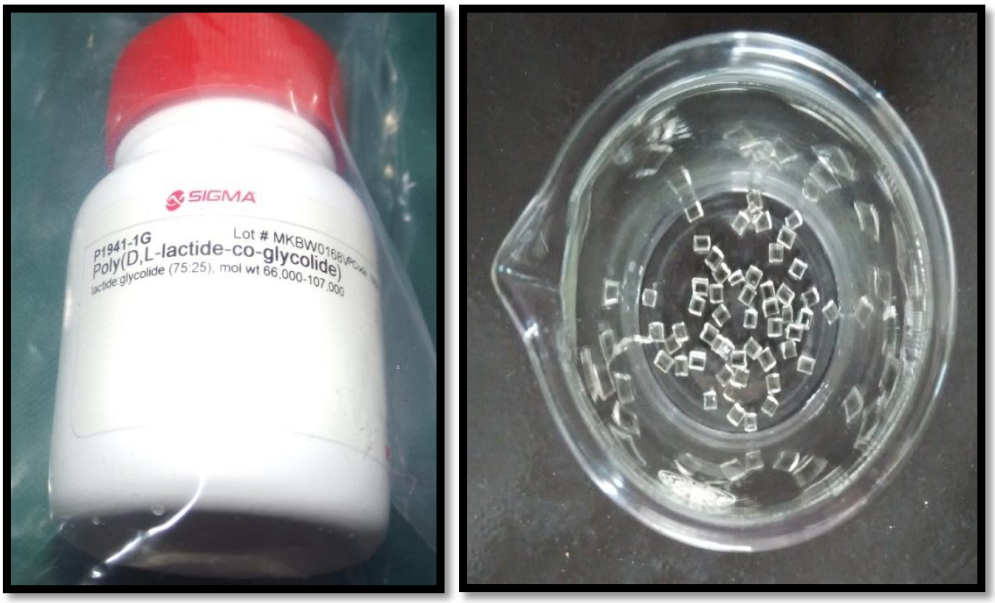
PHOTOGRAPHS

Photograph 1: Surgical Armamentarium

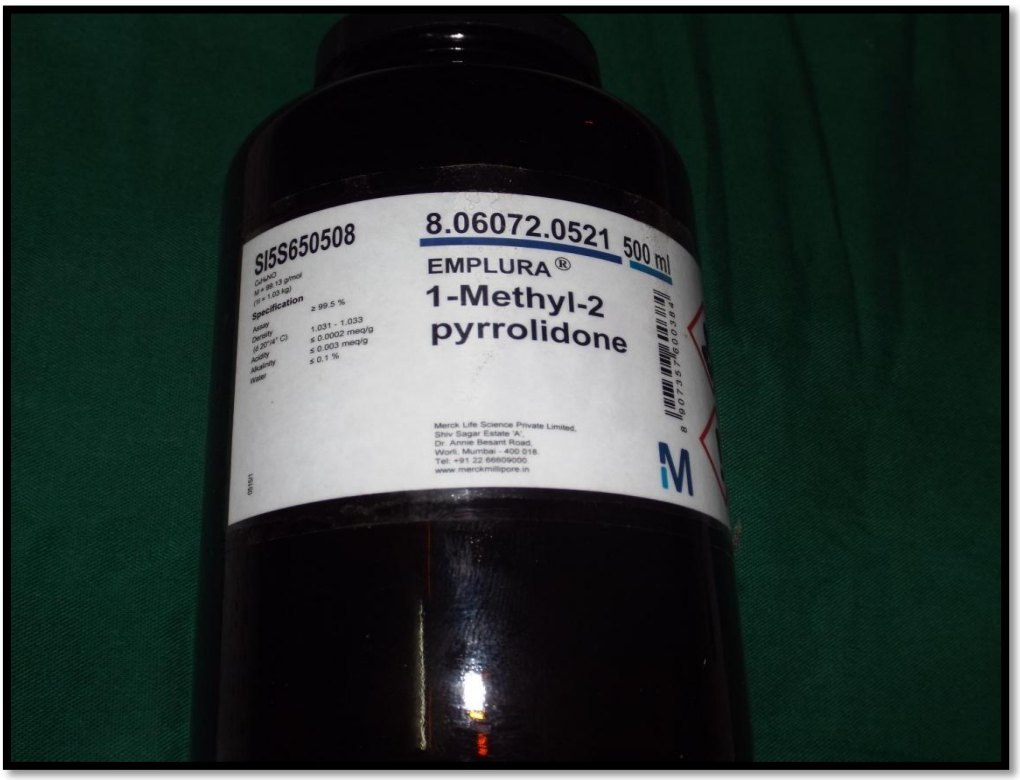
Ingredients of Azithromycin Gel



Photograph 2: Azithromycin Dry Powder



Photograph 3: PLGA (Poly Lactic Co Glycolic Acid)



Photograph 4:1-Methyl-2 pyrrolidone

Azithromycin Gel Preparation

Photograph 5: U-V Spectrophotometer

Photograph 6: Buffer Preparation

Photograph 7: Mechanical Shaker

Photograph 8: Prepared Azithromycin Gel

Photograph 9: Insertion of Azithromycin Gel

Photograph 10: Tetracycline Hydrochloride Fibers

Photograph 11: Insertion of Tetracycline Fibers

Photograph 12: Periodontal Pack Placement

Measurement of Pocket Probing Depth using Acrylic Stent

Photograph 13: Pre-Operative at Baseline

Photograph 14: Post-Operative after 3 months

STATISTICAL ANALYSIS

The statistical analysis was done using the computer software program SPSS version 20.0 (Statistical package for social science version 20). Data is expressed as mean ± standard deviation of the parameters evaluated.

In these three groups, the clinical parameters were evaluated at baseline, 1 month, 2 months and 3 months post-operatively. **Paired t-test** was employed to test the mean changes in scores at different time points within each study groups.

One-way analysis of variance was employed to compare the mean scores between different study groups.

Also Tukey's "Honestly Significant Procedure" was employed to identify the significant groups, if the test of significance in One-Way ANOVA is significant. In all the above statistical tools, the probability value $p \leq 0.05$ was considered as significant.

p value:

The p value or calculated probability was the estimated probability of rejecting the null hypothesis (Ho) of a study question when hypothesis was true. The smaller the p-value, the more significant the result was said to be. All p-values are two tailed and confidence at the 95% level. Differences between two populations were considered when $p \leq 0.05$.

RESULTS

The present clinical study was carried out with the aim to compare and evaluate the efficacy of Scaling and Root Planing (SRP) and SRP in combination with 0.5% Azithromycin gel and, 2 mg Tetracycline fibers in the management of chronic periodontitis.

Sixty patients in the age group between 30 to 45 years were included in the study and were equally distributed into three groups.

Group I - Scaling and Root Planing

Group II - SRP plus 0.5% Azithromycin gel

Group III - SRP plus 2 mg Tetracycline fibers

All the patients who were enrolled in this study returned for scheduled maintenance visits. Clinical parameters were evaluated at baseline, 1 month, two months and three months. All the patients showed good compliance. No adverse reaction was observed in any subject from the study group and no patient reported with any discomfort indicating biocompatibility of Azithromycin gel and Tetracycline fibers.

The observations and results of clinical parameters are summarized in the tables and figures.

Table – I: Comparison of mean scores and percentage changes in plaque index within each group at different time intervals and its significance

Table – II: Comparison of changes in plaque index between the study groups and its significance

Table – III: Comparison of mean scores and percentage changes in bleeding index within each group at different time intervals and its significance

Table – IV: Comparison of changes in bleeding index between the study groups and its significance

Table – V: Comparison of mean scores and percentage changes in probing pocket depth within each group at different time intervals and its significance

Table – VI: Comparison of changes in probing pocket depth between the study groups and its significance

Table – VII: Comparison of mean scores and percentage changes in clinical attachment level within each group at different time intervals and its significance

Table – VIII: Comparison of changes in clinical attachment level between the study groups and its significance.

Clinical parameters:

1. Plaque index:

Group I: The mean plaque index score at 'baseline' was 2.30±0.73, at 1 month it was 1.20±0.77, at 2 months was 0.80±0.62 and at 3 months it was 0.70±0.57.

Group II: The mean plaque index score at 'baseline' was 2.70±0.47, at 1 month was 1.40±0.75, at 2 months was 0.95±0.76 and at 3 month was 0.65±0.67.

Group III: The mean plaque index score at 'baseline' was 2.50±0.51, at 1 month was 1.20±0.83, at 2 months was 0.70±0.73 and at 3 month was 0.75±0.64.

Intragroup comparison:

Group I:

The mean difference of plaque index score between baseline - 1 month was 1.10±0.04 and the percentage of reduction was 47.83 % which was statistically significant.

Baseline – 2 months mean difference was 1.50±0.12 and the percentage of reduction was 65.22 % which was statistically significant.

Baseline – 3 months mean difference was 1.60±0.16 and the percentage of reduction was 69.57 % which shows statistically significant value.

Group II:

The mean difference of plaque index score between baseline - 1 month was 1.30±0.28 and the percentage of reduction was 48.15 % which gives statistically significant value.

Baseline – 2 months mean difference was 1.75±0.28 and the percentage of reduction was 64.81 % which shows statistically significant value.

Baseline – 3 months mean difference was 2.05±0.20 and the percentage of reduction was 75.93% which found to be statistically significant.

Group III:

The mean difference of plaque index score between baseline - 1 month was 1.30±0.32 and the percentage of reduction was 52% which was statistically significant (p=0.0019).

Baseline – 2 months mean difference was 1.80±0.22 and the percentage of reduction was 72% which shows statistically significant value (p=0.0011).

Baseline – 3 months mean difference was 1.75±0.13 and the percentage of reduction was 70 % which shows statistically significant value (p=0.0005).

Intergroup comparison:

The mean reduction of plaque index score between baseline – 1 month was 1.10±0.04 for Group I, 1.30±0.28 for Group II and 1.30±0.32 for Group III which was statistically significant for three groups. But in between three groups it was not statistically significant (p=0.771).

The mean reduction of plaque index score between baseline – 2 months was 1.50±0.12 for Group I, 1.75±0.28 for Group II and 1.80±0.22 for Group III which was statistically significant for three groups. But in between three groups it was statistically non-significant (p=0.516).

The mean reduction of plaque index score between baseline – 3 months was 1.60±0.16 for Group I, 2.05±0.20 for Group II and 1.75±0.13 for Group III which was statistically significant for three groups. But in between three groups it was not statistically significant.

2. Bleeding index:

Group I: The mean bleeding index score at 'baseline' was 3.75±0.72, at 1 month it was 1.55±0.94, at 2 months it was 0.85±0.75 and at 3 months was 0.95±0.76.

Group II: The mean bleeding index score at 'baseline' was 3.65±0.49, at 1 month it was 2.20±1.36, at 2 months it was 2.10±1.12 and at 3 months it was 1.85±1.09

Group III: The mean bleeding index score at 'baseline' was 3.45±0.60, at 1 months was 1.75±1.21, at 2 months it was 1.20±1.06 and at 3 months it was 1.40±0.88.

Intragroup comparison:

Group I:

The mean difference of bleeding index score between baseline - 1 month was 2.20±0.23 and the percentage of reduction was 58.67 % which founds to be statistically significant (p=0.0005).

Baseline – 2 months mean difference was 2.90±0.03 and the percentage of reduction was 77.33 % which shows statistically significant value (p=0.0008).

Baseline – 3 months mean difference was 2.80±0.04 and the percentage of reduction was 74.67 % which was statistically significant (p=0.0002).

Group II:

The mean difference of bleeding index score between baseline - 1 month was 1.45±0.87 and the percentage of reduction was 39.73 % which gives statistically significant value (p=0.0061).

Baseline – 2 months mean difference was 1.55±0.63 and the percentage of reduction was 42.47 % which was statistically significant (p=0.0002).

Baseline – 3 months mean difference was 1.80±0.60and the percentage of reduction was 49.32% which shows statistically significant value (p=0.0001).

Group III:

The mean difference of bleeding index score between baseline - 1 month was 1.70±0.60and the percentage of reduction was 49.28% which was statistically significant (p=0.0001).

Baseline – 2 months mean difference was 2.25±0.45 and the percentage of reduction was 65.22 % which was statistically significant (p=0.0001).

Baseline – 3 months mean difference was 2.05±0.28 and the percentage of reduction was 59.42% which founds to be statistically significant (p=0.0001).

Intergroup comparison:

The mean reduction of bleeding index score between baseline – 1 month was 2.20±0.23 for Group I, 1.45±0.87 for Group II and 1.70±0.60 for Group III which was statistically significant for three groups. But in between three groups it was not statistically significant (p=0.149).

The mean reduction of bleeding index score between baseline – 2 months was 2.90±0.03 for Group I, 1.55±0.63 for Group II and 2.25±0.45 for Group III which was statistically significant for three groups. But in between three groups it was founds to be statistically significant (p=0.004).

The mean reduction of bleeding index score between baseline – 3 months was 2.80±0.04 for Group I, 1.80±0.60 for Group II and 2.05±0.28 for Group III which was statistically significant for three groups. But in between three groups it was statistically significant (p=0.006).

3. Probing Pocket Depth:

Group I: The mean probing pocket depth score at 'baseline' was 5.85±0.75, at 1 month it was 3.25±0.97, at 2 months it was 2.85±0.88 and at 3 months it was 3.45±1.10.

Group II: The mean probing pocket depth score at 'baseline' was 5.90±0.79, at 1 month was 2.85±0.93, at 2 months was 2.75±0.79 and at 3 months was 3.05±0.83.

Group III: The mean probing pocket depth score at 'baseline' was 5.70±0.73, at 1 month was 3.05±1.05, at 2 months was 2.85±0.81 and at 3 months was 3.25±1.02.

Intragroup comparison:

Group I:

The mean difference of probing pocket depth score between baseline - 1 month was 2.60±0.22 and the percentage of reduction was 44.44 % which was statistically significant (p=0.0006).

Baseline – 2 months mean difference was 3.00±0.13 and the percentage of reduction was 51.28 % which was statistically significant (p=0.0012).

Baseline – 3 months mean difference was 2.40±0.35 and the percentage of reduction was 41.03% which gives statistically significant value (p=0.0018).

Group II:

The mean difference of probing pocket depth score between baseline - 1 month was 3.05±0.15 and the percentage of reduction was 51.69% which was statistically significant (p=0.0001).

Baseline – 2 months mean difference was 3.15±0.20 and the percentage of reduction was 53.39% which was found to be statistically significant (p=0.0002).

Baseline – 3 months mean difference was 2.85±0.04 and the percentage of reduction was 48.31% which was statistically significant (p=0.0002).

Group III:

The mean difference of probing pocket depth score between baseline - 1 month was 2.65±0.32 and the percentage of reduction was 46.49% which gives statistically significant value (p=0.0005).

Baseline – 2 months mean difference was 2.85±0.08 and the percentage of reduction was 50.00% which was statistically significant (p=0.0002).

Baseline – 3 months mean difference was 2.45±0.29 and the percentage of reduction was 42.98% which shows statistically significant value (p=0.0003).

Intergroup comparison:

The mean reduction of probing pocket depth score between baseline – 1 month was 2.60±0.22 for Group I, 3.05±0.15 for Group II and 2.65±0.32 for Group III which was statistically significant for three groups. But in between three groups it was not statistically significant (p=0.469).

The mean reduction of probing pocket depth score between baseline – 2 months was 3.00±0.13 for Group I, 3.15±0.20 for Group II and 2.85±0.08 for Group III which was statistically significant for three groups. But in between three groups, the mean reduction in probing pocket depth was statistically non-significant (p=0.676).

The mean reduction of probing pocket depth score between baseline – 3 months was 2.40±0.35 for Group I, 2.85±0.04 for Group II and 2.45±0.29 for Group III which shows statistically significant value for three groups. But in between three groups it was not statistically significant (p=0.358).

4. Clinical Attachment Level:

Group I: The mean clinical attachment level score at 'baseline' was 4.65±0.75, at 1 month was 3.50±0.95, at 2 months was 3.35±0.88 and at 3 months was 4.10±1.07.

Group II: The mean clinical attachment level score at 'baseline' was 4.80±0.70, at 1 month 3.55±0.89 was, at 2 months was 2.65±0.75 and at 3 months was 3.45±0.89.

Group III: The mean clinical attachment level score at 'baseline' was 4.70±0.66, at 1 month was 3.50±0.95, at 2 months was 3.20±1.01 and at 3 months was 3.85±1.04.

Intragroup comparison:

Group I:

The mean difference of clinical attachment level score between baseline - 1 month was 1.15±0.20 and the percentage of reduction was 24.73% which gives statistically significant value (p=0.0039).

Baseline – 2 months mean difference was 1.30±0.13 and the percentage of reduction was 27.96 % which was found to be statistically significant (p=0.0002).

Baseline – 3 months mean difference was 0.55±0.33 and the percentage of reduction was 11.83 % which was statistically not significant (p=0.1679).

Group II:

The mean difference of clinical attachment level score between baseline - 1 month was 1.25±0.19 and the percentage of reduction was 26.04% which shows statistically significant value (p=0.0019).

Baseline – 2 months mean difference was 2.15±0.05 and the percentage of reduction was 44.79% which was statistically significant (p=0.0003).

Baseline – 3 months mean difference was 1.35±0.19 and the percentage of reduction was 28.13% which gives statistically significant value (p=0.0010).

Group III:

The mean difference of clinical attachment level score between baseline - 1 month was 1.20±0.29 and the percentage of reduction was 25.53% which was statistically significant (p=0.0009).

Baseline – 2 months mean difference was 1.50±0.35 and the percentage of reduction was 31.91 % which shows statistically significant value (p=0.0005).

Baseline – 3 months mean difference was 0.85±0.38 and the percentage of reduction was 18.09 % which gives statistically significant value (p=0.0331).

Intergroup comparison:

The mean reduction of clinical attachment level score between baseline – 1 month was 1.15±0.20 for Group I, 1.25±0.19 for Group II and 1.20±0.29 for Group III which was statistically significant for three groups. But in between three groups it was statistically not significant (p=0.946).

The mean reduction of clinical attachment level score between baseline – 2 months was 1.30±0.13 for Group I, 2.15±0.05 for Group II and 1.50±0.35 for Group III which was statistically significant for three groups. But in between three groups it was found to be statistically significant (p=0.017).

The mean reduction of clinical attachment level score between baseline – 3 months was 0.55±0.33 for Group I, 1.35±0.19 for Group II and 0.85±0.38 for Group III which gives statistically significant value for three groups. But in between three groups it was found to be statistically non- significant (p=0.101).

Table 1:

Comparison of mean scores and percentage changes in plaque index within each group at different time intervals and its significance

Time interval	Group I (SRP)					Group II (SRP + Azithromycin)					Group III (SRP + Tetracycline)				
	Mean	± SD	Changes from baseline	% Change	Significance p value	Mean	± SD	Changes from baseline	% Change	Significance p value	Mean	± SD	Changes from baseline	% Change	Significance p value
Baseline	2.30	0.73				2.70	0.47				2.50	0.51			
1 month	1.20	0.77	1.10	47.83	0.0007*	1.40	0.75	1.30	48.15	0.0037*	1.20	0.83	1.30	52.00	0.0019*
2 months	0.80	0.62	1.50	65.22	0.0002*	0.95	0.76	1.75	64.81	0.0007*	0.70	0.73	1.80	72.00	0.0011*
3 months	0.70	0.57	1.60	69.57	0.0003*	0.65	0.67	2.05	75.93	0.0002*	0.75	0.64	1.75	70.00	0.0005*

* Significant

Table 2:

Comparison of changes in plaque index between the study groups and its significance

Time interval	Group I			Group II			Group III			p value	Significant groups
	Mean	± SD	% Change	Mean	± SD	% Change	Mean	± SD	% Change		
0-1 month	1.10	0.04	47.83	1.30	0.28	48.15	1.30	0.32	52.00	0.771	Non significant
0-2 months	1.50	0.12	65.22	1.75	0.28	64.81	1.80	0.22	72.00	0.516	Non significant
0-3 months	1.60	0.16	69.57	2.05	0.20	75.93	1.75	0.13	70.00	0.276	Non significant

Table 3:

Comparison of mean scores and percentage changes in bleeding index within each group at different time intervals and its significance

Time interval	Group I (SRP)					Group II (SRP + Azithromycin)					Group III (SRP + Tetracycline)				
	Mean	± SD	Changes from baseline	% Change	Significance p value	Mean	± SD	Changes from baseline	% Change	Significance p value	Mean	± SD	Changes from baseline	% Change	Significance p value
Baseline	3.75	0.72				3.65	0.49				3.45	0.60			
1 month	1.55	0.94	2.20	58.67	0.0005*	2.20	1.36	1.45	39.73	0.0061*	1.75	1.21	1.70	49.28	0.0001*
2 months	0.85	0.75	2.90	77.33	0.0008*	2.10	1.12	1.55	42.47	0.0002*	1.20	1.06	2.25	65.22	0.0001*
3 months	0.95	0.76	2.80	74.67	0.0002*	1.85	1.09	1.80	49.32	0.0001*	1.40	0.88	2.05	59.42	0.0001*

* Significant

Table 4:

Comparison of changes in bleeding index between the study groups and its significance

Time interval	Group I			Group II			Group III			p value	Significant groups
	Mean	± SD	% Change	Mean	± SD	% Change	Mean	± SD	% Change		
0-1 month	2.20	0.23	58.67	1.45	0.87	39.73	1.70	0.60	49.28	0.149	Non significant
0-2 months	2.90	0.03	77.33	1.55	0.63	42.47	2.25	0.45	65.22	0.004	Highly Significant
0-3 months	2.80	0.04	74.67	1.80	0.60	49.32	2.05	0.28	59.42	0.006	Highly Significant

Table 5:

Comparison of mean scores and percentage changes in pocket probing depth within each group at different time intervals and its significance

Time interval	Group I (SRP)					Group II (SRP + Azithromycin)					Group III (SRP + Tetracycline)				
	Mean	± SD	Changes from baseline	% Change	Significance p value	Mean	± SD	Changes from baseline	% Change	Significance p value	Mean	± SD	Changes from baseline	% Change	Significance p value
Baseline	5.85	0.75				5.90	0.79				5.70	0.73			
1 month	3.25	0.97	2.60	44.44	0.0006*	2.85	0.93	3.05	51.69	0.0001*	3.05	1.05	2.65	46.49	0.0005*
2 months	2.85	0.88	3.00	51.28	0.0012*	2.75	0.79	3.15	53.39	0.0002*	2.85	0.81	2.85	50.00	0.0002*
3 months	3.45	1.10	2.40	41.03	0.0018*	3.05	0.83	2.85	48.31	0.0002*	3.25	1.02	2.45	42.98	0.0003*

* Significant

Table 6:

Comparison of changes in probing pocket depth between the study groups and its significance

Time interval	Group I			Group II			Group III			p value	Significant groups
	Mean	± SD	% Change	Mean	± SD	% Change	Mean	± SD	% Change		
0-1 month	2.60	0.22	44.44	3.05	0.15	51.69	2.65	0.32	46.49	0.469	Non significant
0-2 months	3.00	0.13	51.28	3.15	0.02	53.39	2.85	0.08	50.00	0.676	Non significant
0-3 months	2.40	0.35	41.03	2.85	0.04	48.31	2.45	0.29	42.98	0.358	Non significant

Table 7:

Comparison of mean scores and percentage changes in clinical attachment level within each group at different time intervals and its significance

Time interval	Group I (SRP)					Group II (SRP + Azithromycin)					Group III (SRP + Tetracycline)				
	Mean	± SD	Changes from baseline	% Change	Significance p value	Mean	± SD	Changes from baseline	% Change	Significance p value	Mean	± SD	Changes from baseline	% Change	Significance p value
Baseline	4.65	0.75				4.80	0.70				4.70	0.66			
1 month	3.50	0.95	1.15	24.73	0.0039*	3.55	0.89	1.25	26.04	0.0019*	3.50	0.95	1.20	25.53	0.0009*
2 months	3.35	0.88	1.30	27.96	0.0002*	2.65	0.75	2.15	44.79	0.0003*	3.20	1.01	1.50	31.91	0.0005*
3 months	4.10	1.07	0.55	11.83	0.1679	3.45	0.89	1.35	28.13	0.0010*	3.85	1.04	0.85	18.09	0.0331*

* Significant

Table 8:

Comparison of changes in clinical attachment level between the study groups and its significance

Time interval	Group I			Group II			Group III			p value	Significant groups
	Mean	± SD	% Change	Mean	± SD	% Change	Mean	± SD	% Change		
0-1 month	1.15	0.20	24.73	1.25	0.19	26.04	1.20	0.29	25.53	0.946	Non significant
0-2 months	1.30	0.13	27.96	2.15	0.05	44.79	1.50	0.35	31.91	0.017	Significant
0-3 months	0.55	0.33	11.83	1.35	0.19	28.13	0.85	0.38	18.09	0.101	Non significant

Figure 1: Comparison of mean scores in plaque index within each group at different time intervals

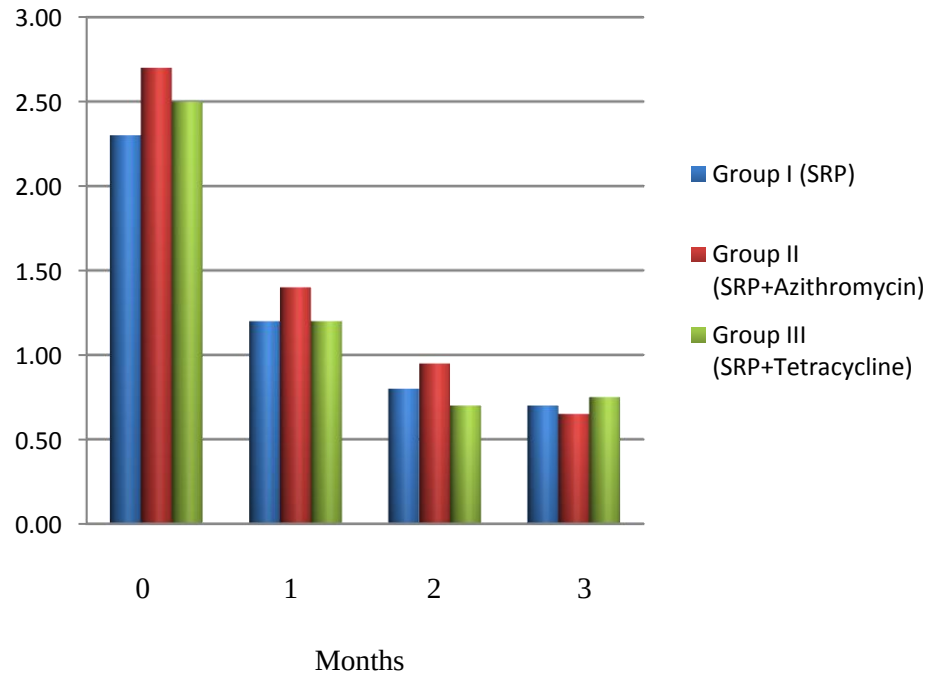


Figure 2: Comparison of changes in plaque index between the study groups and its significance

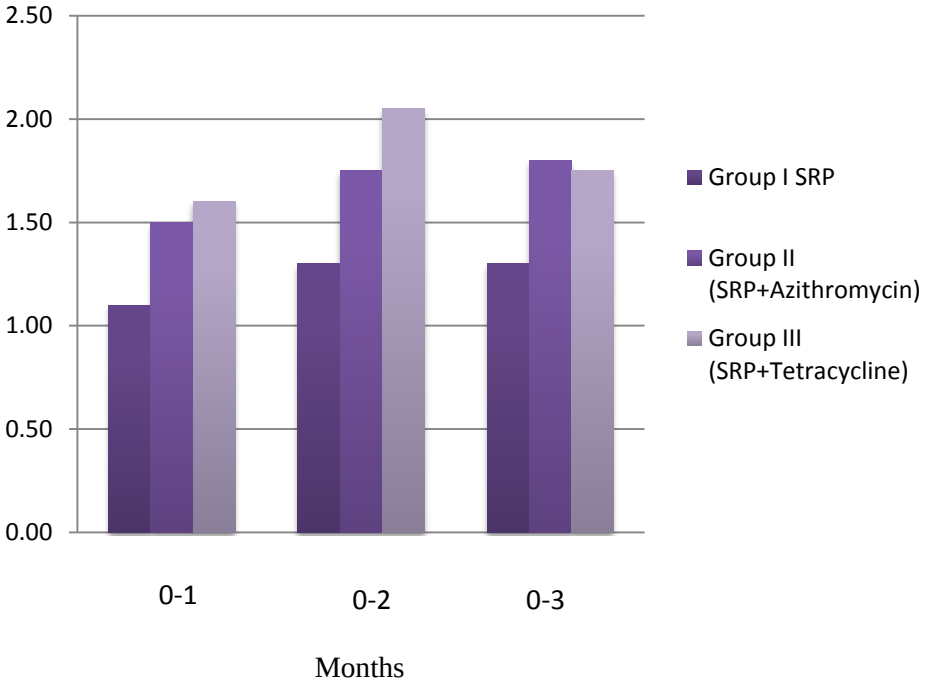


Figure 3: Comparison of mean scores in bleeding index within each group at different time intervals

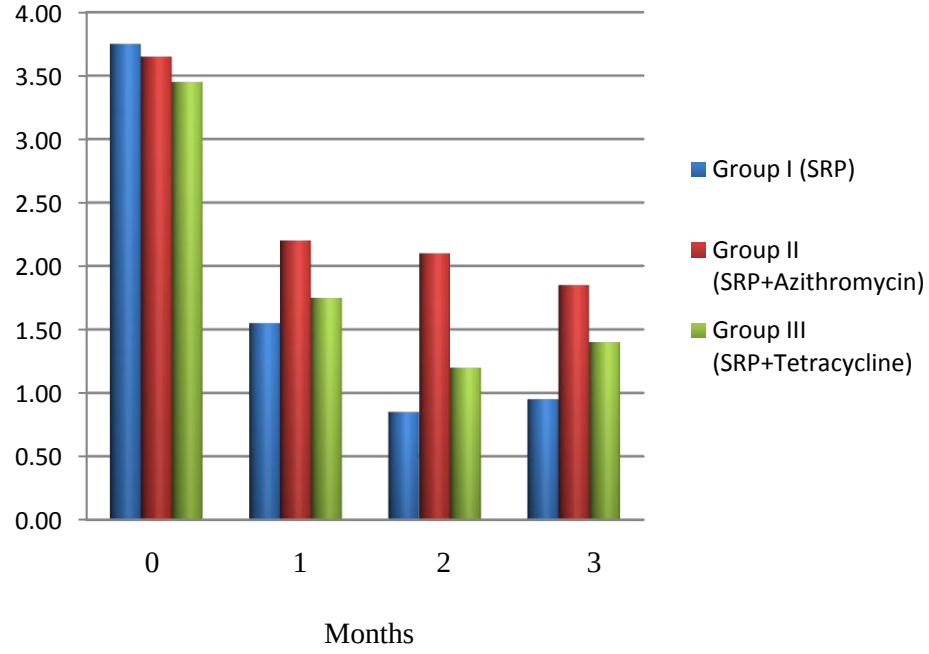


Figure 4: Comparison of changes in bleeding index between the study groups and its significance

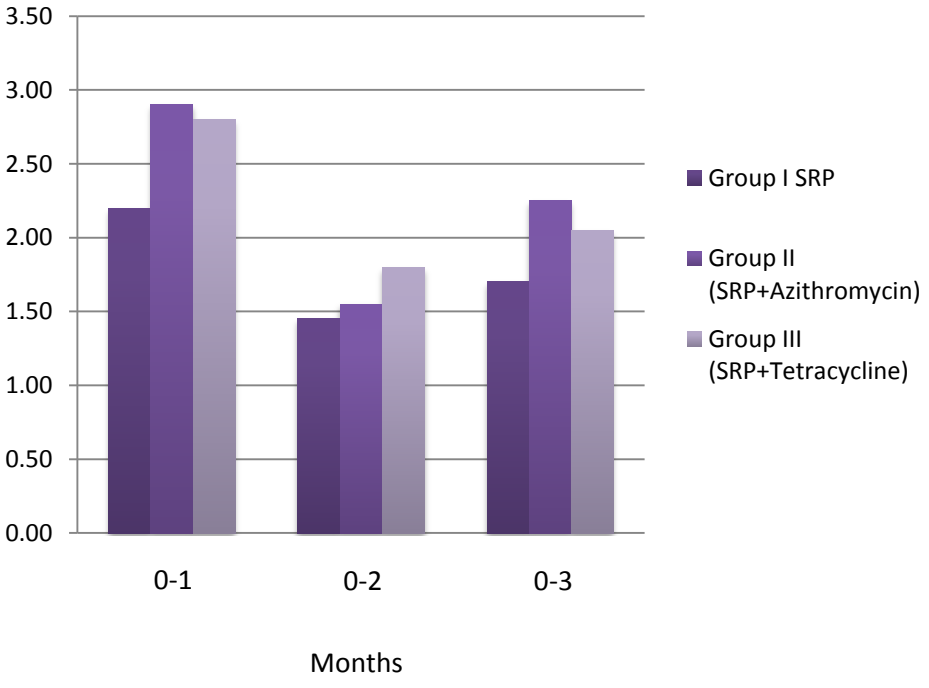


Figure 5: Comparison of mean scores in PPD within each group at different time intervals

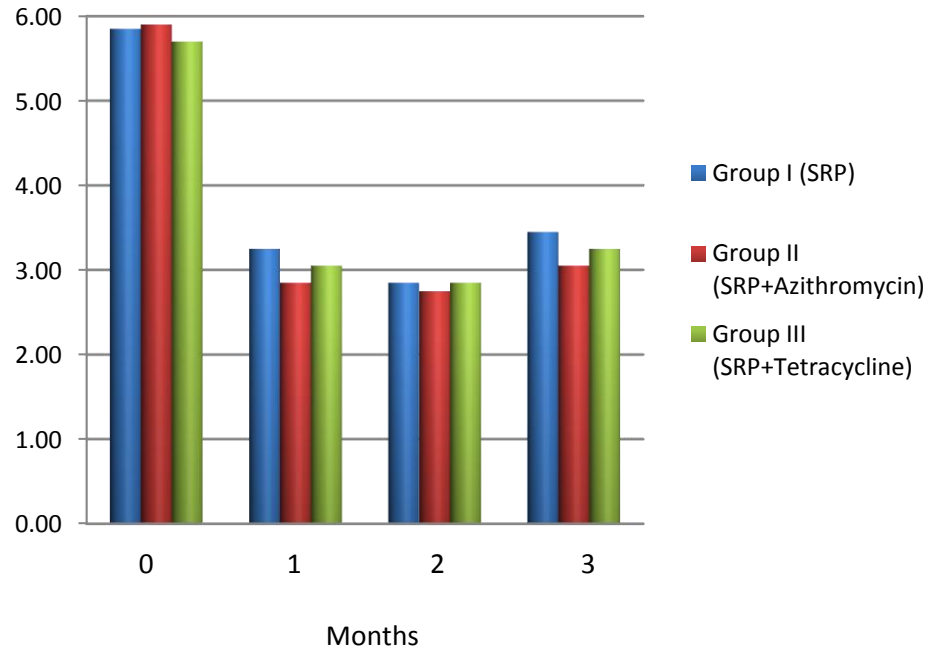


Figure 6: Comparison of changes in PPD between the study groups and its significance

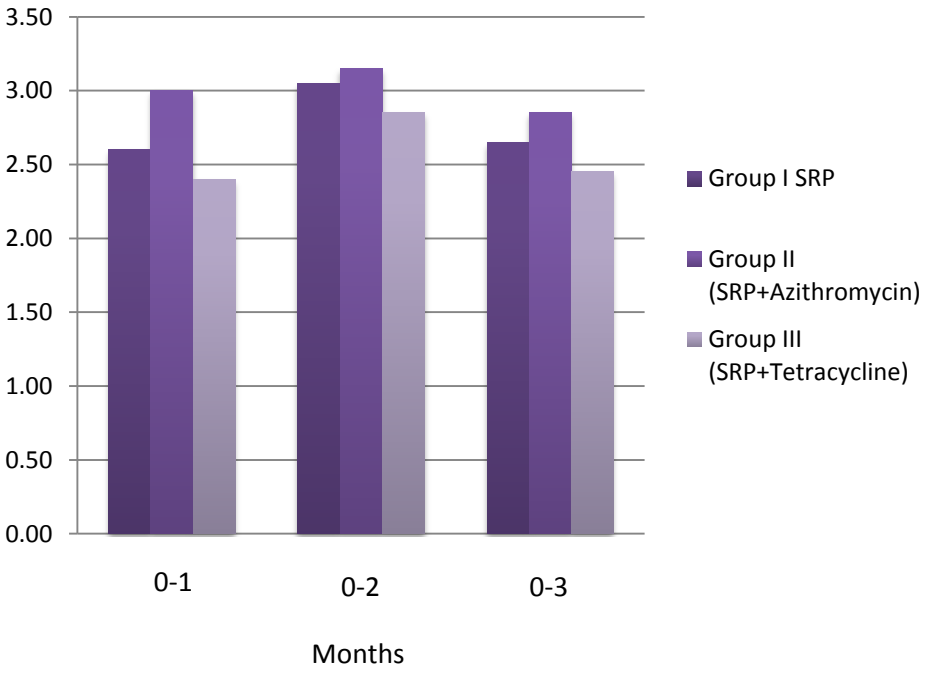


Figure 7: Comparison of mean scores in CAL within each group at different time intervals

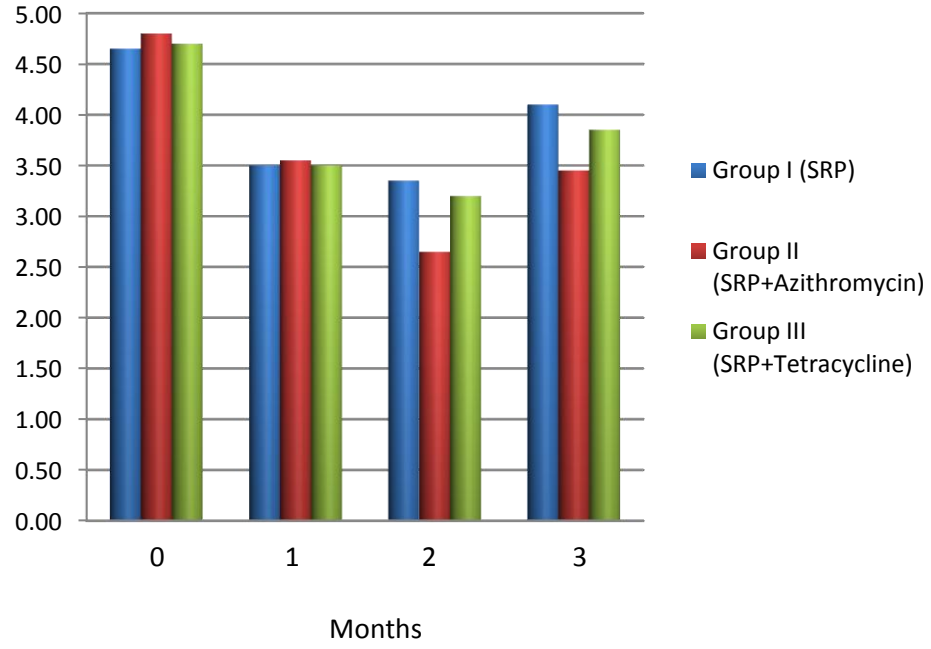
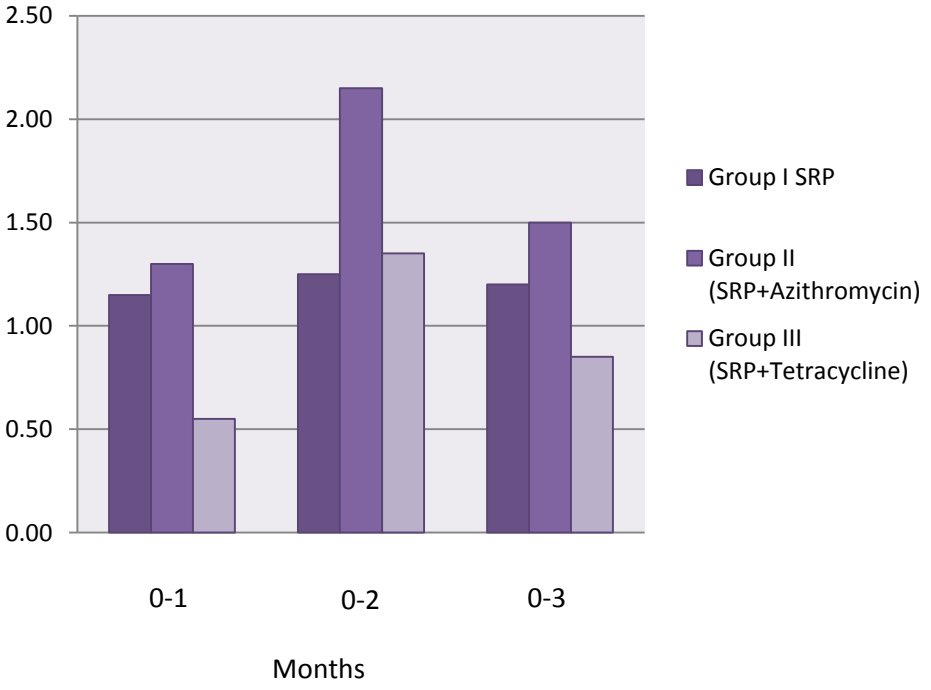


Figure 8: Comparison of changes in CAL between 3 study groups and its significance



DISCUSSION

Microbial plaque is the primary etiologic agent of chronic inflammatory periodontal disease. Scaling and root planing reduces the microbial load but most times, it is not able to remove the tissue invasive pathogens. So, adjunctive chemotherapeutic agents are used to provide the additional benefit over to mechanical debridement systemic administration of antibiotics, significantly improves the clinical outcome although it is associated with inherent adverse effects. To overcome these shortcomings, local drug delivery systems has been developed.

Azithromycin is a semi-synthetic, acid stable macrolide antibiotic. The GCF concentration achieved by locally delivered AZM gel was 2041µg/ml and retained in site for upto 28 days (***Krayer 2010***)[33] whereas tetracycline 1500 µg/ml 10 days (***Gill 1991***)[15]. It has been found useful in the treatment of periodontal infections, because of its rapid absorption, decreased binding to plasma proteins and its increased tissue distribution. In addition to these properties, AZM gets concentrated in fibroblasts and phagocytes. ***Gomi et al., 2007***[17] compared the effects of full-mouth SRP combined with systemic AZM to conventional SRP. In their study, they suggested that full-mouth SRP with systemically administered AZM was a clinically and bacteriologically useful basic periodontal treatment for severe chronic periodontitis patients.

Lactide/glycolide copolymers are used as an effective controlled delivery system because of their biocompatibility and bioabsorbability. ***Robert et al., 1993***[59]

investigated the bioabsorbability and biocompatibility of polylactic membrane and concluded that they showed excellent tissue tolerance with minimal inflammatory reaction. ***Kurtis et al., 2002***[35] tested PLGA membrane with and without metronidazole for guided tissue regeneration without any adverse reaction.

The advantage of PLGA gel used as a vehicle lies in its easy placement, bio - absorbability and does not require any periodontal dressing because it itself filled, swelled and occluded the pocket orifice.

Three months was selected as the duration of this study because the effect of a locally delivered controlled release systems was effective for up to 11 weeks after administration and three months corresponds to the typical recall interval for periodontal patients. (***Soskolne, 1997***)[68]

Goodson et al., 1979[18] studied that the tetracycline filled hollow fibers placed in the gingival sulcus had dramatic effect on the periodontal flora and clinical manifestation of the disease.

Pavia et al., 2003[54] showed that tetracycline and its derivatives minocycline, oxytetracycline and chlortetracycline strongly adsorb to the tooth surfaces retaining the antibacterial activity and are effective to treat the chronic periodontitis.

To the best of our knowledge, there is no published literature comparing the effectiveness of 0.5% AZM *in situ* gel and 2 mg tetracycline fibers as an adjunct to SRP

in the treatment of chronic periodontitis. Hence, in the present study, comparing 0.5% AZM in situ gel and tetracycline fibers was used in the chronic periodontitis patients.

The results of the present study demonstrated a statistically significant reduction in plaque index in the Group I, Group II and Group III compared to baseline at all time intervals. The mean plaque index was 2.30±0.73, 2.70±0.47 and 2.50±0.51 at baseline for the Group I, Group II and Group III. At 3 months, the mean score was 0.70±0.57, 0.65±0.67 and 0.75±0.64 respectively. Similar observations made by ***Eickholz P et al., 2002***[10]***, Jeong et al., 1994***[30]***, Friensen et al., 2002***[13]***, Oosternvalli et al., Vinholis et al., 2001***[75]. Good oral hygiene practiced by the patients throughout the entire study period could have also increased the reduction in plaque. However, on comparison of mean plaque index, scores between Group I, Group II and Group III was significantly non-significant and the findings are in accordance with the study conducted by ***Unsal et al., 1994***[73]. They evaluated the effects of subgingivally delivered 2% chlorhexidine gel and 10% tetracycline paste in periodontal pockets along with scaling and root planing.

Bleeding on probing is an objective sign of inflammation. Research in periodontology suggests that bleeding on probing often is the first sign of gingival inflammation. Reduction in mean bleeding score in groups II and III was highly significant at all time intervals (1.80±0.60, 2.05±0.28 respectively). The same result was obtained by ***Minabe et al., 1989***[44]***, Jaspreet Singh Gill et al., 2011***[15]. The reduction in bleeding is due to resolution of inflammation after SRP. The difference between Group II and Group III failed to reach the level of significance, but there is a greater reduction

in SBI score was observed in the Group II which can be associated with the activity of AZM against periodontal pathogens especially *P. gingivalis,* red complex bacteria. At the end of 3 months in reduction changes in SBI scores reported by ***A.R. Pradeep et al., 2008***[1].

Reduction in pocket probing depth and gain in clinical attachment level are the major clinical outcomes measured to determine the success of a treatment. A significant reduction in PD and CAL gain were found within the groups II and III compared to baseline at all time intervals. When comparing the group I, II and III, the reduction in PD was statistically significant at each period and PD was significant at the end of 3 months between group II and III ($p<0.0001$).

In the present study, Group II and III the reduction in PD was 2.40±0.35mm, 2.85±0.03mm and 2.45±0.20mm. In a study by ***Haffajee et al., 1997***[25], the number of sites showing an increase in attachment gain > 2 mm and PD reduction in post therapy was significantly greater in SRP plus systemic metronidazole group. ***Gomi et al., 2007***[13]***, Mascarenhas et al., 2005*** [39] observed the same results in their study.

In Group II, this may be due to higher uptake of AZM by fibroblasts and acute phase reactant cells. AZM is released and delivered in higher concentration to phagocytosed bacteria at the site of infection.

In Group III, this may be due to collagenase inhibition property, anti-inflammatory effect and inhibition of bone resorption by tetracycline and their property to promote attachment of fibroblasts to root surfaces.

However, limitations of this study were that it was a short term study, but the findings were encouraging and it justifies the need for long term study to evaluate the true value. Further long term trails using different vehicles and concentration of azithromycin desired to comment as its application in periodontal disease as an adjunct to scaling and root planing to support the observations of this study.

SUMMARY & CONCLUSION

The present study was conducted as a comparative clinical evaluation of 0.5%Azithromycin gel and 2mg of tetracycline fibers as an adjunct to scaling and root planing in the treatment of chronic periodontitis. A total of 60 subjects were selected for the study. They were randomly divided into 3 groups as follows

Group I - Scaling and root planing

Group II - Scaling and root planing+0.5%Azithromycin *in-situ* gel

Group III - Scaling and root planing+2mg Tetracycline fibers

Thus, each group had 20 subjects. The clinical parameters were assessed at baseline, 1month, 2 months, 3months and the values were subjected to statistical analysis.

The following conclusion was drawn from the study:

- Both Azithromycin gel and Tetracycline fibers were well tolerated by the periodontal tissues during the course of the study.
- There was a definite improvement in clinical parameters in all the 3 groups (ie) SRP, SRP+0.5% Azithromycin gel, SRP+2mg Tetracycline fibers from baseline to 3 months.
- Adjunctive use of Azithromycin gel and Tetracycline fiber reveal significant reduction in clinical parameters at 3 months when compared to SRP alone.
- But there was statistically no significant difference between AZM & Tetracycline group.

From this study, it has been observed that both AZM gel and Tetracycline fibers are an effective means of non-surgical treatment modality for the management of chronic periodontitis. Additionally, in case of AZM the better handling property, higher GCF concentration achieved (2041µg/ml), longer period of substantivity (upto 28 days), improved patient compliance and the absence of the need for use of periodontal dressing for the retention proved AZM as a promising adjunct to conventional scaling and root planing, which would enhance the effectiveness of the treatment.

Within the limit of the present study, all the three modalities of treatment were efficient in improving the clinical parameters and there is no statistically significant difference between AZM & Tetracycline group. In future, clinical trials with larger samples and long- term follow-up period may be employed to further explore the potential benefit of AZM as a local drug delivery agent.

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Annexures

CERTIFICATE OF AZITHROMYCIN GEL PREPARATION

From

Prof. ELANGO,
Head of the Department,
Department of Pharmaceutics,
College of Pharmacy,
Madras Medical College,
Chennai.

To

The Chairman,
Institutional Ethical Committee,
Tamil Nadu Government Dental
College and Hospital,
Chennai.

Respected Sir,

Sub : Preparation of Azithromycin gel – Reg.

The Department of Pharmaceutics, College of Pharmacy, Madras Medical College, Chennai has prepared and provided the Azithromycin gel using Azithromycin Powder, Poly lactic-co-glycolic acid (PLGA) and N-Methyl-2-Pyrolidinone for fulfilling the needs of the thesis titled "A comparative clinical evaluation of subgingivally delivered 0.5% Azithromycin gel and 2mg tetracycline hydrochloride fibers as an adjunct to scaling and root planing in the treatment of chronic periodontitis", by Dr.S.Annapoorani, II Year PG, Dept. of Periodontics, Tamilnadu Government Dental College and Hospital, Chennai.

Thanking you,

Yours sincerely,

Place : Chennai
Date : 20/06/16.

(Prof.ELANGO)

PROFESSOR AND HEAD
DEPARTMENT OF PHARMACEUTICS
COLLEGE OF PHARMACY
MADRAS MEDICAL COLLEGE
CHENNAI-600 003

PROFORMA FOR TREATMENT GROUP

Date : OP No.: S.No.:

Name : Age : Sex:

Occupation : Income :

Address : Phone Number :

CHIEF COMPLAINTS AND DURATION:

HISTORY OF PRESENT ILLNESS:

PAST MEDICAL HISTORY:

PAST DENTAL HISTORY:

FAMILY HISTORY :

PERSONAL HISTORY :

a) Oral Hygiene Practices :
b) Habits :
c) Menstrual History :
d) Menopause :
e) H/o. Stress Factor :

GENERAL EXAMINATION

a) Extra-Oral Examination

b) Examination of Lymphnodes

INTRA-ORAL EXAMINATION WITH CLINICAL FINDINGS:

Buccal mucosa:

Vestibule:

Hard palate:

Soft palate:

Tonsils:

Tongue:

Floor of the mouth:

Teeth:

Decayed

Missed

Filled teeth

Gingiva

Plaque index

18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38

Bleeding Index

18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38

Probing depth and attachment loss in millimetre

Maxillary:

CAL																
PPD																
	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
PPD																
CAL																

Mandibular:

CAL																
PPD																
	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38
PPD																
CAL																

Investigations:

1. Biochemical / Haematological Investigation :
2. Others :

   Blood Pressure :

   Test Dose for L.A:

RADIOGRAPHIC EVALUATION

Intra-Oral Periapical Radiograph/ Orthopantomogram (IOPA/OPG)

PROVISIONAL DIAGNOSIS

PROGNOSIS

TREATMENT PLAN

FITNESS FOR TREATMENT

TREATMENT DONE

DATE : PROCEDURE : SIGNATURE :

MAINTENANCE PHASE

EVALUATION AFTER - 1 MONTH

EXTRA-ORAL/INTRA-ORAL EXAMINATION

Gingiva

Plaque index

18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38

Bleeding index

18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38

Probing depth and attachment loss in millimetre

Maxillary:

CAL																
PPD																
	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
PPD																
CAL																

Mandibular:

CAL																
PPD																
	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38
PPD																
CAL																

MAINTENANCE PHASE

EVALUATION AFTER - 2 MONTHS

EXTRA-ORAL/INTRA-ORAL EXAMINATION

Gingiva

Plaque index

18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38

Bleeding index

18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38

Probing depth and attachment loss in millimetre

Maxillary:

CAL																
PPD																
	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
PPD																
CAL																

Mandibular

CAL																
PPD																
	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38
PPD																
CAL																

MAINTENANCE PHASE

EVALUATION AFTER - 3 MONTHS

EXTRA-ORAL/INTRA-ORAL EXAMINATION

Gingiva

Plaque index

18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38

Bleeding index

18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38

Probing depth and attachment loss in millimetre

Maxillary:

CAL																
PPD																
	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
PPD																
CAL																

Mandibular

CAL																
PPD																
	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38
PPD																
CAL																

SIGNATURE OF THE PROFESSOR

ஆராய்ச்சி பற்றிய தகவல் படிவம்

ஆராய்ச்சி மேற்கொள்பவர்: மருத்துவர். அன்னபூரணி

வழிநடத்துபவர்: மருத்துவர்: K . மாலதி. M. D. S.

ஆராய்ச்சி நிறுவனத்தின் பெயர்: தமிழ்நாடு அரசு பல் மருத்துவக் கல்லூரி மற்றும் மருத்துவமனை, சென்னை.

ஆராய்ச்சியின் தலைப்பு: நாள்பட்ட பல் ஈறு நோய்க்கு அசித்ரோமைசின் அரைத்திண்மக் கரைசல் மற்றும் டெட்ராசைக்ளின் இழைகளைப் பல் மற்றும் பல்லின் வேர் சுத்தம் செய்தல் சிகிச்சையுடன் உபயோகித்தல் - ஒரு ஒப்பீட்டு மருத்துவ மதிப்பீடு

ஆராய்ச்சியின் நோக்கம்: நாள்பட்ட பல் ஈறு நோய்க்கு பல் மற்றும் பல்லின் வேர் சுத்தம் செய்தல் சிகிச்சையை ஒன்று, இரண்டு மற்றும் மூன்று மாத காலத்திற்கு மதிப்பீடு செய்தல்.

செய்முறை: கீழ்கண்ட ஆய்வுகள்/பரிசோதனைகள் உங்களுக்காக செய்யப்படும்:

- வாய் பரிசோதனை
    - உட்புறம்
    - வெளிப்புறம்
- வழக்கமான இரத்தப் பரிசோதனை
- உங்களின் கையிலிருந்து இந்தப் பரிசோதனைக்காக 5 மில்லியளவு (ஒரு மேஜைக் கரண்டி அளவு) இரத்தம் எடுக்கப்படும்.
- நோயுற்ற பகுதியின் ஊடு கதிர்படம்.
- சிகிச்சை தேவைப்படும் பல்லின் அளவானது அல்ஜினேட் அச்சு கொண்டு எடுக்கப்படும்.
- ஒவ்வாமை ஏற்படுகிறதா என்பதைத் தெரிந்து கொள்ள 0.5 மில்லி 2% லிக்னோகெயின் மயக்க மருந்து உங்களின் கையில் பரிசோதனைக்காகக் கொடுக்கப்படும். பின்பு, நோயுற்ற பகுதியில் மயக்க மருந்து கொடுக்கப்படும்.
- அல்ட்ரா சோனிக் ஸ்கேலர் மற்றும் கைக் கருவிகள் பயன்படுத்தி பல் மற்றும் பல்லின் வேர் சுத்தம் செய்யப்படும். உப்புநீர் கொண்டு நோயுற்ற பகுதி சுத்தம் செய்யப்படும்.
- 0.2 மில்லி அசித்ரோமைசின் அரைத்திண்மக் கரைசல் அல்லது 2 மி. கிராம் டெட்ராசைக்ளின் ஹைட்ரோ குளோரைடு இழைகள் நோயுற்ற பகுதியின் ஈறுக்கடியில் வைக்கப்படலாம்.

பங்கேற்பதினால் வரக்கூடிய பக்க விளைவுகள்: வலி, வீக்கம் மற்றும் பயன்படுத்தும் பொருட்களினால் சில நேரங்களில் ஒவ்வாமை ஏற்பட வாய்ப்புண்டு. அதற்காகத் தேவைப்படும் மருந்துகளும் மருத்துவமும் வழங்கப்படும்.

பங்கேற்பதினால் விளையும் நன்மைகள்:

1. உங்களின் நாள்பட்ட பல் ஈறு நோய்க்கு சிகிச்சை அளிக்கப்படும்.

இரகசிய காப்பு: உங்களை பற்றிய குறிப்புகள் பிறர் அறியா வண்ணம் ஆராய்ச்சி முடியும் வரை இரகசியமாக பாதுகாக்கப்படும். அதை வெளியிடும் நேரங்களில் எந்த தனி அடையாளங்களும் வெளிப்பட வாய்ப்பு கிடையாது.

தன்னார்வ பங்கேற்பு: இந்த ஆராய்ச்சியில் பங்கு பெறுவது தங்களின் தனிப்பட்ட முடிவு மற்றும் இந்த ஆராய்ச்சியில் இருந்து நீங்கள் எப்போது வேண்டுமானாலும் விலகிக்கொள்ளலாம். தங்களின் இந்த திடீர் முடிவு உங்களுக்கோ அல்லது ஆராய்ச்சியாளருக்கோ எந்த வித பாதிப்பும் ஏற்படுத்தாது என்பதை தெரியப்படுத்துகிறோம்.

நோயாளியின் பெயர்

கையொப்பம்/கைரேகை

ஆராய்ச்சி தொடர்புடைய தகவல்களுக்கு

மரு. சு. அன்னபூரணி

F - 4, தாமரை குடியிருப்பு, முதல் தெரு, சென்னை – 600035

தொலைபேசி எண்: 9940648870

பங்கேற்பாளரின் உரிமை தொடர்புடைய தகவல்களுக்கு:

மரு. திலகவதி சுப்ரமணியன்

தலைவர், நிறுவன நெறிமுறைகள் குழு

தமிழ்நாடு அரசு பல் மருத்துவக் கல்லூரி மற்றும் மருத்துவமனை, சென்னை

Participant Information Sheet

Investigator: Dr. S. Annapoorani Guide: Dr. K. Malathi M.D.S

Title of the study: A COMPARATIVE CLINICAL EVALUATION OF SUBGINGIVALLY DELIVERED 0.5% AZITHROMYCIN GEL AND 2 MG TETRACYCLINE HYDROCHLORIDE FIBERS AS AN ADJUNCT TO SCALING AND ROOT PLANING IN THE TREATMENT OF CHRONIC PERIODONTITIS.

Name of the research institution: Tamilnadu Government Dental College & Hospital, Chennai.

The investigator, Dr. S. Annapoorani under the guidance of Dr K.Malathi M.D.S is conducting a study as titled above with aim to do a comparative evaluation of azithromycin gel and tetracycline fibers usage in the gum along with scaling and root planing in chronic periodontitis.

1. **Procedure: The following examination/investigation will be done for you.**
   - Intra oral examination, Extra oral examination
   - Routine blood test – 5ml(1 table spoon) of blood will be drawn from your hand
   - X-ray will be taken for the diseased site
   - Model for your teeth will be prepared by taking alginate impression
   - A test dose of 0.5ml of 2% Lignocaine will be injected below the skin in your arm
   - Under local anesthesia deposits on your teeth will be removed with ultrasonic scaler and hand instrument. Saline irrigation will be done at the diseased site. 0.2 ml of azithromycin gel or 2 mg of tetracycline fiber may or may not be placed in the diseased site. The further clinical evaluation will be performed at day one, one month, two month and three months after the procedure.
2. **Risk of participation:**
   There maybe pain/swelling/allergic reaction to materials used for which adequate drugs will be given.
3. **Benefits of participation**
   Treatment for your diseased status (chronic periodontitis) will be given.
4. **Confidentiality:**
   The identity of the patients participating in the research will be kept confidential throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.
5. **Participant's rights:**
   Taking part in the study is voluntary. You are free to decide whether to participate in the study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled. The results of this study will be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.
6. **Compensation: Nil**
7. **Contacts:**

For queries related to the study:	**Contact details regarding rights of the participant:**
Primary Investigator: Dr.S.ANNAPOORANI	Dr. Thilakavathy Subramanian
Contact Details: F4, Lotus colony, 1st Street, Nandanam, Chennai -600035	The Chairperson, Institutional Ethical committee
Phone number: 9940648870	Tamilnadu Govt. Dental College & Hospital, Chennai

ஒப்புதல் படிவம்

ஆராய்ச்சியின் தலைப்பு

நாள்பட்ட பல் ஈறு நோய்க்கு அசித்ரோமைசின் அரைத்திண்மக் கரைசல் மற்றும் டெட்ராசைக்ளின் இழைகளை பல் மற்றும் பல்லின் வேர் சுத்தம் செய்தல் சிகிச்சையுடன் உபயோகித்தல் - ஒரு ஒப்பீட்டு மருத்துவ மதிப்பீடு

பெயர் : புறநோயாளி எண்:

வயது/பால்: ஆராய்ச்சி சேர்க்கை எண்:

முகவரி :

தொலைபேசி :

நான் ..... வயது ..... என்னுடைய சுயநினைவுடனும் மற்றும் முழு சுதந்திரத்துடனும் இந்த மருத்துவ ஆராய்ச்சியில் என்னை சேர்த்துக்கொள்ள ஒப்புதல் அளிக்கிறேன்.

<u>கீழ்க்காணப்படும் நிபந்தனைகளுக்கு நான் சம்மதிக்கிறேன்:</u>

- நான் இந்த ஆராய்ச்சியின் நோக்கம் மற்றும் செயல்முறைகள் பற்றி முழுமையாக தெரிவிக்கப்பட்டுள்ளேன்.
- இந்த பரிசோதனைக்காக பற்கள் மற்றும் ஈறுகளில் சுத்தம் செய்யும் சிகிச்சை செய்ய வேண்டியுள்ளதாக அறிகிறேன்.
- சிகிச்சையின் போது டெட்ராசைக்ளின் இழைகள் உபயோகிக்க சம்மதிக்கிறேன்
- என் உடல்நலம் பாதிக்கப்பட்டாலோ அல்லது எதிர்பாராத வழக்கத்திற்கு மாறான நோய் குறிகள் தென்பட்டாலோ அதனை விலக்குவதற்கும் முழு உரிமை உள்ளதாக அறிகிறேன்.
- நான் ஏற்கனவே உட்கொண்ட மற்றும் உட்கொள்கின்ற மருந்துகளின் விபரங்களை ஆராய்ச்சியாளரிடம் தெரிவித்துள்ளேன்.
- என் மருத்துவ குறிப்பேடுகளை இந்த ஆராய்ச்சியில் பயன்படுத்திக்கொள்ள சம்மதிக்கிறேன். இந்த ஆராய்ச்சி மையமும் ஆராய்ச்சியாளரும் என்னுடைய விபரங்கள் அனைத்தையும் இரகசியமாக வைப்பதாக அறிகிறேன்.

நோயாளியின் பெயர்	கையொப்பம்	தேதி
ஆராய்ச்சியாளரின் பெயர்	கையொப்பம்	தேதி

Informed Consent Form

A COMPARATIVE CLINICAL EVALUATION OF SUBGINGIVALLY DELIVERED 0.5% AZITHROMYCIN GEL AND 2 MG TETRACYCLINE HYDROCHLORIDE FIBERS AS AN ADJUNCT TO SCALING AND ROOT PLANING IN THE TREATMENT OF CHRONIC PERIODONTITIS

Participant ID No:

"I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions I have asked have been answered to my satisfaction. I consent voluntarily to participate as a participant in this study and understand that I have the right to withdraw from the study at any time without in any way it affecting my further medical care."

Date	Name of the participant	Signature/thumb impression of the participant

[The literate witness selected by the participant must sign the informed consent form. The witness should not have any relationship with the research team; If the participant doesn't want to disclose his / her participation details to others, in view of respecting the wishes of the participant, he / she can be allowed to waive from the witness procedure (This is applicable to literate participant ONLY). This should be documented by the study staff by getting signature from the prospective participant]

"I have witnessed the accurate reading of the consent form to the potential participant and the individual has had opportunity to ask questions. I confirm that the individual has given consent freely"

Date	Name of the witness	Signature of the witness

Date	Name of the interviewer	Signature of the interviewer